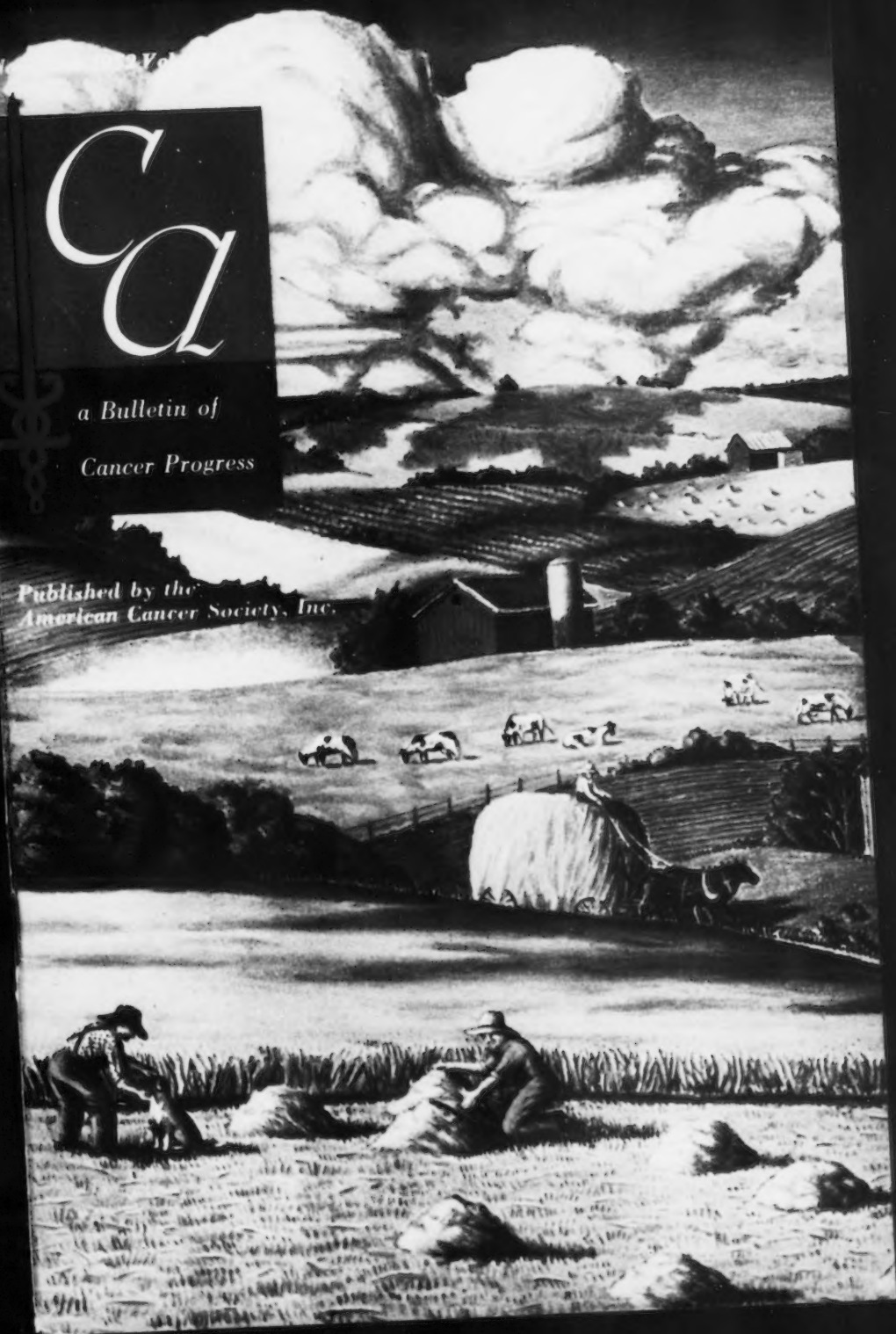


# Ca

a Bulletin of  
Cancer Progress

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*from chimney  
sweep and  
smelter to  
radiologist  
and atomic  
chemist*

In the seventeenth century, Ramazzini, the father of industrial medicine, was the first to note the occurrence of the rough, keratotic skin of fishermen. Two centuries later Unna re-described this precancerous condition of the sailor's skin caused by excessive exposure to solar rays, thus opening the whole subject of radiation as an etiological factor in cancer.

Pott, in 1775, connected etiologically the scrotal cancers of chimney sweeps with their occupational exposure to soot. Early in the nineteenth century, the etiology of scrotal cancers of the copper and tin smelters of Cornwall was shown to be the occupational responses to arsenic fumes. Later in that century, occupational cancers of the skin in the paraffin workers in Saxony and in Scotland and in workers in tar, pitch, and crude oil were described. These industrial discoveries of the causes of skin cancer led to the study of experimental carcinogenesis, benzanthracene being found by Kennaway in 1924 to cause cancer when applied repeatedly to the skin.

Thus, some cancers of the skin bear the distinction of known etiologies and have opened the way to research leading to what little we now

know of the direct causes of cancer. In addition, most skin cancer differs from cancer of other organs by being least malignant and most accessible, and therefore easiest and earliest diagnosed, most adequately treated, and most readily cured.

Cancer and precancer of the skin accordingly offer the greatest opportunity to industrial and general practitioners for early diagnosis, adequate therapy, and total control. They can also contribute to the control of skin cancer by preventing excessive contacts with known carcinogenic agents—chemicals, radiation, and other chronic irritants—counseling fair-complexioned sun-worshipping patients not to "go out in the noonday sun" excessively and patients who are farmers, sailors, gardeners, roofers, stokers, steel and foundry, and roentgen-ray, radium, and atomic workers to wear protective clothing and to use appropriate protective devices. The early occupational skin cancer of roentgenologists and roentgen-ray technicians was eliminated immediately upon recognition of the hazard and provision of appropriate safeguards.

At present, in the larger medical centers, 95 per cent of skin cancers are cured. This cure rate and that in the smaller communities can be further increased by alertness of the first physician to see the lesion—the general practitioner.

*Cover*

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# NEWSLETTER

NOVEMBER, 1952

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## NOTES FROM THE AUSTRIAN CHAPTER OF THE INTERNATIONAL COLLEGE OF SURGEONS

Schoenbauer's (Vienna) statistical material on heredity in cancer extends over three and four generations. Mandl (Vienna) recommended for breast carcinoma, radical operation in combination with castration, hormone therapy, and postoperative irradiation. Chiari (Vienna) reported 86 per cent of stomach-carcinoma cases are localized in the antrum; 82 per cent had infiltrated all layers without causing symptoms indicating surgery; lymph nodes were involved in approximately half the cases. Abrahamson (Stamford) reported 56 per cent of more than 700 stomach carcinomas inoperable, and 45 per cent of the patients died during hospitalization. He considers the usual two-thirds resection palliative, with total gastrectomy giving better prospect of cure. Huber (Vienna) reported that all seventeen cases of medulloblastoma operated upon died within one year. (In a majority of brain metastases, bronchial carcinoma was the primary tumor.) Klemme (St. Louis) said he achieved 96 per cent correct brain-cancer diagnoses with radioactive diiodofluorescein. Ventriculography gives satisfactory results in 85 per cent. Despite the great risk, he prefers to treat medulloblastoma in children surgically, followed by roentgen-ray radiation. The mortality is 17 per cent. Kraus (Vienna) reported that 50 per cent of spinal tumors proved amenable to radical surgery. Novotny (Vienna), in the light of advances in chemotherapeutic, antibiotic, and anesthetic drugs, favors extirpation of the cancerous larynx. He seldom uses roentgen-ray therapy in operable cases. His one-stage method leaves the musculature in place in case of endolaryngeal carcinoma. Herbst (Graz), elaborating on the electrosurgical methods of Keysser, described electrodes adapted to special uses. Tissues infiltrated by cancer are coagulated by heat and the lymph vessels closed. This prevents extension of the cancer tissue by surgical intervention and minimizes bleeding. The method is used especially in carcinoma of parenchymatous organs and of the skin.

## HERE AND THERE IN CANCER RESEARCH

Glutamic acid determinations in blood serum don't look so good as a cancer blood test, Tufts investigators report. . . . Rotation therapy with M.I.T.'s 2-million-volt roentgen-ray apparatus continues to yield satisfactory results (293 of 455 patients treated were without clinical evidence of disease, although recurrences may be expected as time passes); an enormous variety of cancers have responded to treatment. . . . Yale experiments in transplanting embryonic endocrine organs homologously in humans and heterologously in animals continues to look promising after more than two years of intensive study. . . . University of Pennsylvania results with high voltage roentgenograms for early detection of lung cancer have proved to be promising in this important diagnostic field. . . . Worcester Foundation for Experimental Biology scientists are studying urinary steroid excretion patterns in men and women, and preliminary results indicate that they differ considerably in youth and age. . . . A University of Minnesota thesis indicates that bone receives relatively greater radiation damage from low roentgen-ray tube voltages than from high, another point in favor of supervoltage therapy. . . . Yale's Long and Fry have transplanted pituitary anterior-lobe tissues to the eyes of hypophysectomized rats and found the tissues capable of producing ACTH and male gonadotropic hormone and supporting growth. . . . Larson of Columbia University College of Physicians and Surgeons has tested the antibody response of cancer patients to pneumococcus capsular polysaccharides and found patients with chronic lymphatic leukemia and multiple myeloma showed little or no antibody formation, chronic myeloid leukemias showed a high response, and acute leukemias produced exceedingly large amounts of antibody. Cortisone impaired the last mentioned response.

Columbia University Institute of Cancer Research recently doubled its laboratory space and increased facilities for patients by one third. Research goes on in 125 specialized laboratories. More than 5000 patients were treated during the past year in the 300-bed Francis Delafield Hospital for Cancer. New departments include Anesthesiology, Physical Medicine and Rehabilitation, Microbiology, and Research in Animal Diseases.

(Continued after page 220)

**C**  
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NOVEMBER 1952

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# KEEPING UP WITH

Digests from current literature of special importance  
in diagnosis and treatment . . .

## Hemisulfur Mustard for Advanced Cancer

Hemisulfur mustard, which is one thirteenth as toxic as HN<sub>2</sub>, was studied in thirty-one patients with advanced cancer, who were either inoperable and unsuitable for radiation therapy, or had received the maximum dose, or had become refractory to further radiation. Most of them were in the terminal stages of cancer. Eight of thirteen patients with peritoneal carcinomatosis and ascites (seven with ovarian carcinoma and one with scirrhous carcinoma of the stomach) showed a striking decrease in the accumulation of the ascitic fluid for a period of two to six months. One did not reaccumulate ascitic fluid for ten months. Two other patients with prostatic carcinoma showed a drop from abnormally high levels of serum acid phosphatase. Subjectively all ten patients showed increased appetite, greater activity, decreased pain and discomfort, and in general felt more fit a week or more after termination of the injections; in all cases the subjective improvement was of limited duration. These patients lived from two to nineteen months with an average survival time of six months, whereas seventeen of the twenty-one patients who were not benefited by hemisulfur mustard died within two months.

Malaise, weakness, nausea, and vomiting uniformly followed the administration of hemisulfur mustard. In the first patients treated, the injections were followed by local thrombophlebi-

tis with marked pain, swelling, and tenderness. Subsequently the drug was injected through polyvinyl tubing inserted into the vena cava via the saphenous vein or into the subclavian vein via the median basilic vein. This eliminated the complications. A few patients showed signs of neurotoxicity. No other systemic toxicity was observed.

*Seligman, A. M.; Rutenburg, A. M.; Persky, L., and Friedman, O. M.: Effect of 2-chloro-2'-hydroxydiethyl sulfide (hemisulfur mustard) on carcinomatosis with ascites. Cancer 5: 354-363, March, 1952.*

## Lymph-Node Smears in Diagnosis

A smear from the cut surface of a lymph node provides more rapid means of determining possible involvement of regional lymph nodes than does frozen-section technique. Out of 242 smears (checked by later histological sections of the same node area), 219 were satisfactory and gave a 98.6 per cent accuracy in diagnosis; there were three false negatives, no false positives. The lymph nodes were obtained at operation on various genital cancers, mostly carcinoma of the cervix or vulva.

*Dearing, R.: Diagnosis of malignant involvement of lymph nodes by a smear technique. J. Obst. & Gynaec. Brit. Emp. 59: 385-387, June, 1952.*

## Premalignant Phase of Endometrial Cancer

A study of curettings of the endometrium, made a few to many years prior to the diagnosis of endometrial carcinoma, has thrown light on the early and/or precancerous phases of these tumors. The curettings in sixteen

# CANCER

cases made prior to the diagnosis of endometrial carcinoma fell into three categories. 1. In three cases the review showed that carcinoma had been present when the first curettings were made but these had been misdiagnosed as hyperplasia. 2. In two cases the original curettings showed normal endometrium; these antedated the later carcinoma by nineteen and twenty-two years. 3. Atypical or adenomatous hyperplasia of the endometrium was found to have been present in all of the curettings from the other eleven patients in the study—curettings obtained between one and eighteen and a half years prior to the diagnosis of carcinoma. The author concludes that, at present, unexplained adenomatous hyperplasia should probably be considered a precancerous lesion in the postmenopausal uterus.

*Speert, H.: The premalignant phase of endometrial carcinoma. Cancer 5: 927-944, Sept., 1952.*

## Metastatic Prostatic Carcinoma in Bone Marrow

Nineteen of fifty-seven patients with prostatic carcinoma (forty-nine histologically proved) were found to have metastatic cells in the bone marrow on routine bone-marrow aspiration; the cells were found equally often in the marrow from the sternum and from the ilium. Five of the nineteen patients with positive smears had no roentgenographic evidence of metastasis. The other fourteen showed metastases roentgenographically as did nine other patients who had negative smears. Of the various adjunctive laboratory procedures, the alkaline phosphatase was the most useful in diagnosis, being elevated in seventeen of the twenty-eight

with metastases and four of the twenty-nine without; the acid phosphatase was elevated in fifteen with, and one without, metastases; no determination was made in nine. No correlation was found between grade of malignancy and metastatic spread. The authors conclude that, since adequate bone-marrow examination can be done in one hour or less by a competent person, it should be done on patients with prostatic carcinoma who are being considered for radical surgery.

*Clifton, J. A.; Philipp, R. J.; Ludovic, E., and Fowler, W. M.: Bone marrow and carcinoma of the prostate. Am. J. M. Sc. 224: 121-130, Aug., 1952.*

## Occupational Cancer—Control Measures

Control measures directed against known and suspected occupational carcinogenic agents must include the workers in the production and use of these agents, the population living in the environment of the plants with carcinogenic hazards, and the general public. A great deal of educational work has to be done in medical circles so that physicians become aware of the existence of occupational hazards and learn to discover and evaluate precancerous conditions, thereby aiding industrial management in controlling occupational cancer effectively from a medical standpoint.

A prerequisite to a rational and intelligent occupational-cancer control would be the recognition of carcinogenic agents and exposures. The term "environmental-carcinogen pattern" is interpreted to mean the wide range of abnormal symptoms presented by a worker population in the presence of a carcinogenic agent. Excessive inci-

dence of cancer in special groups of workers and shifts in the sex ratio of cancer incidence furnish other important clues as to an occupational-cancer hazard. In the case of lung cancers, an increasing preponderance of squamous-cell and anaplastic cancers over adenocarcinomas favors an occupational or exogenous origin. This may have an etiological significance and may indicate not only that an injurious agent is present but that it occurs in the form of a gas, vapor, mist, dust, or fume. Information of this type is of the utmost importance in the subsequent development of effective preventive and precautionary measures. Workers should be informed of the hazards connected with their work. Where possible, the occupational carcinogenic agent should be completely eliminated by using or producing suitable noncarcinogenic substitutes. A closed system of production is another way of eliminating cancer hazards in industry. Good housekeeping in plants and personal hygiene of the workers are other ways to reduce hazards. An attempt should be made to develop either production methods through which the production of carcinogenic contaminants is avoided or to remove or destroy the carcinogenic portion in the hazardous product.

Hueper, W. C.: *Occupational cancer hazards in American industries*. A.M.A. Arch. Indust. Hyg. 5: 204-208, March, 1952.

### **Does Chronic Ulcerative Colitis Lead to Cancer?**

How much does the probability of malignant change affect the prognosis of a given case of chronic ulcerative colitis and just how important is this danger as an indication for surgical resection of the large intestine? In 226 verified cases, ulcerative colitis acquired in the second decade of life and continuing until the third decade proved a real hazard as far as malignant change is concerned. In itself, however, the danger is not sufficient to demand surgical extirpation of the

colon and rectum without other indications. Most patients with active colitis persisting for ten or more years are subjects for surgery even without the added hazard of cancer. If an ileostomy has been necessary, the danger of malignant change would seem to be sufficient to warrant total colectomy. In patients with chronic ulcerative colitis who are under medical observation and treatment, the policy of examining them at intervals for evidence of malignant change is tempered by the fact that under these circumstances cancer is incurable by the time it has developed to the point at which it can be diagnosed.

Kiefer, E. D.; Eyttinge, E. J., and Johnson, A. C.: *Malignant degeneration in chronic ulcerative colitis*. *Gastroenterology* 19: 51-57, Sept., 1951.

### **Progesterone in Breast Cancer**

Only two of twenty patients with advanced cancer of the breast treated with progesterone showed objective and subjective improvement: in one calcification of metastatic bony lesions of several months' duration occurred (she has responded dramatically and longer to testosterone propionate); in the other, pleural effusion was absent for ten months, although subjective improvement lasted only six months. Progesterone was given in a dosage of 100 mg. intramuscularly three times weekly and was continued until there was objective evidence of progression of the disease. A severe local reaction followed administration of progesterone in aqueous solution—in some instances sterile draining abscesses associated with severe pain; this was not observed with progesterone in oil. None of the patients showed increase in weight or feeling of well-being. The urinary-excretion patterns of eleven patients are given. About 10 per cent of the administered steroid was recovered. One showed a rise in 17-ketosteroid excretion comparable to that noted during testosterone propionate treatment. There was an increase in urinary pregnanediol and a decrease in urinary-

gonad-stimulating hormone during progesterone therapy. It is possible that the conversion of progesterone to pregnanediol may be abnormal in patients with cancer of the breast.

Gordon, D.; Horwitt, B. N.; Segaloff, A.; Muri-son, P. J., and Schlosser, J. V.: *Hormonal therapy in cancer of the breast. III. Effect of progesterone on clinical course and hormonal excretion.* *Cancer* 5: 275-277, March, 1952.

### **Uterine Cancer**

Early detection of cervical and endometrial cancer can be made possible only by clearing away a few old misconceptions from the minds of both physicians and laymen. Until proved otherwise, abnormal bleeding of any type at or near the menopause should be considered organic. In postmenopausal bleeding following hormone administration, complete diagnostic studies are in order. Irrespective of age, religion, or virginity, all patients with abnormal uterine bleeding should have a thorough diagnostic examination.

Using the physician's office as the first line of defense, cervical carcinoma in situ can be detected in its incipient stages and then absolute cure approaches 100 per cent. Fourteen per cent of the first 100 cases with cancer of the cervix diagnosed in the Cytology Laboratory at the University Hospitals (Western Reserve) were shown to have early carcinoma of the cervix solely on the basis of exfoliative cytology. It is believed that visualization and palpation alone are not sufficient to rule out cancer of the cervix. Papanicolaou smears should be obtained on all patients. However, it must be borne in mind that they are an additional aid and not a substitute for visualization and palpation or for diagnostic curettage and cervical biopsy when there are suspicious symptoms.

It is unwise to cauterize the cervix unless smears and biopsy have failed to show cancer. In the event of a positive smear and a negative biopsy, sharp conization of the cervix is in order, as well as thorough curettage of the endometrium and endocervix. In the pres-

ence of abnormal bleeding during pregnancy, biopsy is frequently necessary and not fraught with too much danger. Positive or negative findings by hysterosalpingography or endometrial biopsy must be corroborated by thorough uterine curettage. There is no clinical or experimental evidence that curetting a cancer of the endometrium can disseminate the tumor.

Except for in situ or microscopically detected early invasive cancer, the treatment of choice for all cervical cancer is radiation. For carcinoma in situ of the cervix, a radical total hysterectomy is recommended, which should include a wide portion of the broad ligaments and an ample cuff of vagina. Cauterization or conization of the cervix, amputation of the cervix, or simple hysterectomy are not adequate treatments for carcinoma in situ.

Surgery alone in the treatment of cancer of the endometrium has resulted in a 50 to 55 per cent five-year salvage. More recently, preoperative roentgen-ray treatment and/or intrauterine radium, followed in four to eight weeks by total hysterectomy and bilateral salpingo-oophorectomy, has increased the five-year salvage to 67 to 90 per cent.

Scott, R. B., and Reagan, J. W.: *Misconceptions about uterine cancer.* *GP* 4: 35-42, Dec., 1951.

### **Leukoplakia and Cancer of the Vulva**

The incidence of carcinoma associated with leukoplakia of the vulva has been variously reported as being from 21.3 to 55 per cent. In the author's series of thirty-four patients there were twelve cases of associated vulvar carcinoma, 35.3 per cent. A comparative group of thirty-three patients with leukoplakia of the mouth revealed but one instance of associated mouth cancer. The two groups were comparable for age at menarche, age at menopause, and onset of leukoplakia—sixth decade. In the literature, leukoplakia of the vulva appears gen-

erally to be attributed to deficient ovarian activity; on the other hand, leukoplakia of the mouth is attributed to faulty dietary assimilation or vitamin-B deficiency. The author raises the question of the abuse of estrogens as contributing to the possible etiology of associated vulvar carcinoma and cites a case report in support of his view.

The author warns against the indiscriminate use of estrogens in menopausal therapy—such patients being of the age at which leukoplakia of the vulva most commonly ensues—and also suggests that the importance of leukoplakia and kraurosis vulvae as precancerous conditions has perhaps not been sufficiently widely recognized. He, himself, has found vitamin E effective enough that he has abandoned all use of estrogens as a therapeutic agent in women presenting symptoms of the menopause.

*Christy, C. J.: The abuse of estrogens in the treatment of leukoplakia of the vulva. Am. J. Obst. & Gynec. 63: 1133-1138, May, 1952.*

### **The General Surgeon and Breast-Cancer Surgery**

How closely can the results of surgery of the breast, performed in a small general hospital, compare with the results obtained in large hospitals and clinics in which breast surgery is done, not by the general surgeon, but by the specialist? The authors report on treatment in a 350-bed hospital, in which surgery for tumors of the breast was performed by a staff of seven senior surgeons.

In the years 1938 through 1945, 153 patients received a diagnosis of carcinoma or sarcoma of the breast; ten had secondary lesions and are not considered in the survey; of the remaining 143, seven were considered totally inoperable—leaving 136 treated by surgery with or without supplemental roentgen-ray therapy. The hospital incidence of all breast lesions was 0.72 per cent and of malignant breast lesions, 0.25 per cent. Ten cases were discovered on routine examination;

sixty-two (43.1 per cent) were seen within two weeks to two months of onset of symptoms; the rest, at periods varying from three to forty-eight months after onset. The smallest tumor was 0.3 sq. cm., the great majority (71 per cent) 9.0 sq. cm. or less in surface area. Of the 136 operations performed, ninety-two were radical mastectomies, five were subradical (pectoralis minor muscle left in situ), thirty-five were simple mastectomies, and four were local excisions. About half of the simple mastectomies were performed for palliation only. The four local excisions were biopsies and, following a review of permanent sections and the establishment of a definite diagnosis, the patients refused further surgery.

The rate of recurrence was 21.9 per cent. The over-all absolute five-year-survival rate was 42.7 per cent; for those having radical mastectomy it was 47.8 per cent. The authors conclude that their five-year-survival rate following radical mastectomy does not compare too badly with that obtained by some of the large centers; they also feel that this is a selective rate and the comparable figure is the lower five-year absolute survival (42.7 per cent)—and that it is lower owing to the inadequacy of simple mastectomy when done for actual definitive therapy, as occurred in about half of their cases so treated.

The authors warn that the active general surgeon should not identify his results too closely with those reported by the larger clinics and teaching institutions where so much of surgical therapy is departmentalized.

*Zellinger, J. J., and Adie, G. C.: Carcinoma of the breast; results of treatment in a small general hospital. Ann. Surg. 135: 173-183, Feb., 1952.*

### **Methylandrostenediol in Breast Cancer**

Patients with advanced carcinoma of the breast who have improved on testosterone propionate have usually shown a decrease in creatinuria. Methylandro-

stenediol was selected for clinical trial because it could be expected to affect creatine metabolism and because of its lack of androgenicity. The usual dosage was 100 mg. three times weekly; two received 100 mg. daily. Objective regression of the lesions was noted in only two of twenty-four patients: in one for five and a half months; in the other, eight weeks. Only the soft-tissue lesions were affected, whereas testosterone has been particularly effective in patients with skeletal metastases. Many patients complained of local pain and swelling at the site of injection and two had local sterile abscesses. The patients showed a greater increase in creatinuria than did those on testosterone propionate therapy who failed to improve; gonadotropic-hormone excretion was unaffected. Four patients showed values for gonadotropic-hormone excretion below those expected for their endocrine status.

*Segaloff, A.; Gordon, D.; Horwitz, B. N.; Schlosser, J. V., and Murison, P. J.: Hormonal therapy in cancer of the breast. II. Effect of methylandrostenediol on clinical course and hormonal excretion. Cancer 5: 271-274, March, 1952.*

### Periosteal Chondroma

Periosteal chondroma is a distinctive benign cartilage tumor that apparently originates in the periosteum. Although the authors have seen only six cases, five of these were seen in one year.

The tumor has been found on the bones of the hand and the foot as well

as on the bones of the extremities, such as the tibia and humerus. The tumor is of comparatively small size, slowly growing, and develops beneath the periosteal connective tissue and characteristically erodes and induces considerable sclerosis of the contiguous cortical bone. It can be differentiated from osteochondroma and solitary enchondroma roentgenographically. The symptoms are pain, gradual swelling, and local tenderness that range from a few months to as much as ten years in duration. On palpation the tumor is firm, usually small, and slightly tender and if located near a joint may produce some limitation of movement. Surgically it presents as a rubbery, firm, lobulated cartilage tumor adherent to the periosteum; it may be partially nestled within the gouged-out underlying cortex, which is extremely resistant to curettage. Conservative surgical extirpation and curettement of the eroded sclerosed cortical base is the usual recommended treatment. Block excision is feasible if the tumor has involved a long limb bone and is substantially larger than it would be on the phalanx of the finger.

One of the patients reported has been followed more than three years, but thus far there has been no indication of any tendency to local recurrence following surgical extirpation.

*Lichtenstein, L., and Hall, J. E.: Periosteal chondroma; a distinctive benign cartilage tumor. J. Bone & joint Surg. 34A: 691-697, July, 1952.*

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Albucasis, Cordova's celebrated Spanish-Arabian surgeon, born A.D. 1013, in *Collectio*, Book II, Chapt. III, had his doubts about the value of surgical treatment for cancer. If the cancer lies in a locality where it can be grasped in toto like the mammary gland, and especially if not fully developed, operation may be attempted. Though he says "As for me I have never been able to cure a case nor have I known of one who has."



## a glance . . .

**one-minute abstracts  
of the current literature  
on cancer . . .**

### **Treatment of Skin Cancer**

There are three major groups of skin cancer: squamous-cell carcinoma, basal-cell carcinoma, and melanoblastoma. It is stressed that early diagnosis and complete destruction of the primary skin cancer are very important. Of 374 cases of skin cancer, 268 of the lesions were less than 2 cm. in diameter and showed no evidence of local extension or metastasis. This group was treated by (1) local infiltration anesthesia, (2) biopsy of part of the tumor for microscopic study, (3) electrocoagulation of the tumor, (4) curettage of the entire lesion down to the normal tissue, (5) electrocoagulation of a few millimeters of the surrounding tissue, and (6) roentgen-ray therapy of 1000 units, 100 kv. P., 5 ma., 1 mm. aluminum filtration once a week for three weeks. The second group of 106 cases of skin cancer were treated by surgical excision and consisted of twenty-three basal-cell carcinomas, sixty-nine squamous-cell carcinomas, and fourteen malignant melanomas. Previous treatment had been given in 23 per cent of the cases. In this group treatment consisted of: (1) local excision, (2) local excision and application of skin graft, (3) excision with

prophylactic lymph-node dissection, (4) excision with therapeutic lymph-node dissection, (5) amputation.

The four-year-cure rate in the first group was 97.4 per cent (there were seven recurrences and no deaths). In the second group there were thirteen recurrences and six known deaths over a three-year period, a curability rate of 82.08 per cent.

An infinitely higher number of permanent cures are obtained today in the treatment of skin cancer than was the case twenty years ago.

*Sawyer, K. C., and Woodburne, A. R.: The treatment of skin cancer. Arizona Med. 9: 26-27, Jan., 1952.*

### **Occupational Cancer of the Skin**

All dermatologists should recognize the possibility that occupational cancer of the skin, though rare, can and does exist. The United States is not so far advanced as other countries in the study, control, and prevention of occupational skin cancers, hence cases go unreported. Needless to say the majority of tar and oil cancers have not been reported, while the long latent period of arsenic cancer may account in part for the small number of reported cases caused by arsenic. According to a recent report there were

seventy-one tar and pitch cancers of the skin, sixty-two grease and oil cancers, forty-five roentgen-ray cancers, and eighteen arsenic cancers on record.

Occupational cancer of the skin is liable to develop in workers exposed to soot, pitch, tar, shale oil, arsenic, creosote, solvents, paraffin wax, and repeated injury. Cancerous transformation in the skin (most frequently of the face, hands, and scrotum) often results from prolonged heat or overexposure to roentgen rays. Diagnosis is based on the patient's history and clinical examination, confirmed by biopsy report.

The author reports personal cases of skin cancer in a coal-tar distiller, a gardener using arsenic sprays, a coal-tar distiller working with creosote, a grease-pit worker, and various cases of cancer of the skin arising as the result of trauma. Epitheliomas of the skin may appear as the result of minute repeated injuries. Cancerous transformation may also occur in a wound resulting from severe crushing injury with subsequent infection and prolonged treatment. The author does not believe that a single trauma ever caused cancer of the skin.

Prevention of occupational skin cancer rests on the individual physician who actually sees the patient. A careful history of the patient should reveal whether or not his occupation is a factor in producing the cancer. The New York State Occupational Cancer Committee is prepared to trace any suspected case of occupational skin cancer to its source and to conduct thorough investigations.

*Downing, J. G.: Cancer of skin and occupational trauma. J.A.M.A. 148: 245-252, Jan. 26, 1952.*

### **Carcinoma of the Lip**

A study extending over thirty years was made of 835 cases of malignant epithelial lesions of the lip. It was found that squamous-cell carcinoma of the lip in young patients, treated in the early stages, resulted in a high rate of cure. The three-year-cure rate in this

group of patients and a small number of older civilians and retired soldiers was 92.3 per cent; the five-year-cure rate was 82.1 per cent. There is a tendency toward increasing incidence of lip cancer with advancing age, the average age of World War II soldiers with carcinoma of the lip being thirty-seven years but that of the entire Army, twenty-five years. Since less than 1 per cent of the patients were Negroes, it is almost conclusively evident that carcinoma of the lip is infrequent in Negro males. Of 594 patients with data, 560 used tobacco in some form but only 15 per cent of these smoked pipes; 38 per cent of a control group of men of comparable average age but without carcinoma of the lip were pipe smokers. Among those for whom data were available, it was found that patients with ruddy or fair complexions predominated in the series regardless of the geographic region of birth or whether indoor or outdoor workers; that a majority were born in states south of the 40th degree of latitude, had served longest in United States areas receiving 60 per cent or more of the annual sunshine, and had served six months or longer in subtropical areas overseas. All this indicates that patients with ruddy and fair complexions are more sensitive to the effects of actinic radiation than are those with medium or dark complexions. In 778 of 821 lesions in 801 patients, the site was the lower lip. Multicentric lesions occurred in twenty patients. Excision was performed in 85 per cent of the lesions, combined with roentgen rays in 8 per cent, with radium in 2 per cent, and with both roentgen rays and radium in 1 per cent. The presence of senile elastosis on the mucous-membrane side, the skin side, or both in 83.5 per cent of an age group as young as the one in this study suggests the influence of certain factors in increasing the local age changes, possibly sunlight. Since only 14 per cent of the lesions were Grade III or IV, this study added confirmation to the belief that squamous-cell carcinoma of

the lip is essentially a tumor of low-grade malignancy, and prognosis is excellent provided detection is early and treatment adequate.

Bernier, J. L., and Clark, M. L.: Squamous cell carcinoma of the lip: a critical statistical and morphological analysis of 835 cases. *Mil. Surgeon* 109: 379-405, Oct., 1951.

### Treatment of Skin Carcinoma

More than 3000 persons in the United States died of skin cancer in one recent year. Inadequate initial treatment is blamed for this shocking death rate. Other factors include delay on the part of the patient to seek medical attention, failure of the physician to recognize the condition, and the omission of biopsy.

Three fundamental rules must be followed for successful treatment of cutaneous carcinoma: (1) performance of biopsy; (2) complete excision of the growth when surgically treated, and (3) calculation of the tissue dose for the base of the lesion, taking into consideration the total length of the treatment period in treatment by irradiation.

Cutaneous carcinoma may be cured equally well by surgical, radium, or roentgen-ray therapy. In this series of 1204 cases the early lesions, 1.0 cm. in diameter or less, were almost always treated by surgical excision for biopsy and simultaneous cure. Epitheliomas of the hands, feet, legs, scalp, the forehead, and ears were usually excised, since radiation is not well tolerated over superficial bone or cartilage. Large lesions, 5.0 cm. or more in diameter, in any location, were usually treated by excision, with or without skin graft. Surgery or radiation is used on lesions of intermediate size, depending on the individual case. Roentgen-ray therapy by protraction and fractionation with 100 kv. equipment and planned on the time-dose relationship was found to be the best form of irradiation. Topical radium therapy is frequently used in early superficial growths. In interstitial radium therapy, dosage is determined

by the dimensions of the growth, irrespective of histopathology.

Recurrent cutaneous carcinoma is predominantly treated by surgical excision and, if necessary, plastic repair. It is concluded that recurrent carcinoma originates from malignant cells that are more or less incorporated in scar tissue. If the disease reappears within 1.0 cm. of the margin of the scar during the five-year period it was considered recurrent.

Seven of the 1204 patients died from cutaneous carcinoma; six had from three to twenty-two recurrences; five had the disease for more than ten years. Three of these seven could be given palliative treatment only.

Sharp, G. S., and Binkley, F. C.: *The treatment of carcinoma of the skin.* *Am. J. Roentgenol.* 67: 606-619, April, 1952.

### Medical Arsenical Skin Cancers

Eight cases of arsenical epithelioma of medicinal arsenical origin were seen during a two-year period; the authors also report one case of benign superficial epitheliomatosis. Diagnosis depends on cutaneous manifestations of chronic arsenism (hyperpigmentation or melanosis and keratoses) and a positive history of exposure to medicinal arsenic. The malignant lesions usually assume the gross features of the different types of cutaneous epithelioma but occasionally may simulate the lesions of superficial epitheliomatosis. Other lesions may simulate Bowen's disease. Sometimes more than one type appears in the same person. The average age at onset for arsenical keratoses is 32 years and for arsenical epitheliomas 51 years; the range in time from first exposure to appearance of the lesions is wide. There is apparently no regular relationship between the amount and duration of arsenical medication and the occurrence of the disease. In one case treatment lasted only one month. There was no instance of associated cancer of the internal organs in this series to date.

Arsenical keratoses must be considered potentially malignant lesions.

Surgical excision is the treatment of choice for all suspicious lesions showing recent changes in size or growth rate or having surface ulceration. Electrocautery is more practical for widespread multiple keratoses but should be preceded by punch biopsy.

Prognosis in cases of arsenical epithelioma is better than with the usual type of skin cancer. The choice of therapy depends upon the location and

extent of the lesions. Surgery is preferable for lesions of the extremities. Roentgen-ray therapy may be used for small, early cases occurring around the nose, eyes, or ears because of the better cosmetic results. Radical dissection of regional nodes is indicated for metastatic squamous-cell carcinoma.

*Arhelger, S. W., and Kremen, A. J.: Arsenical epitheliomas of medicinal origin. Surgery 30: 977-986, Dec., 1951.*

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#### **Excerpts from: Malignant Melanoma — A Clinicopathological Analysis of the Criteria for Diagnosis and Prognosis**

The epidermal junctional nevus, or the junctional component of the compound nevus, is the source of the melanocarcinomas of the skin and mucous membranes, the rare malignant blue nevus excepted, of course. Only a small percentage of the junctional nevi, however, become malignant. The observation that the pigmented nevi of the soles, palms, and genitalia were junctional or compound nevi furnished a basis for understanding the vulnerability of the moles in these regions to melanocarcinomatous change; for this reason, when feasible, moles in these locations should be prophylactically excised, preferably prior to puberty. Approximately one of every ten cutaneous melanocarcinomas is superimposed on compound nevi or juvenile melanomas.

The "juvenile melanomas" of children may easily be confused by pathologists with the fatal melanocarcinomas; there are special histological features of the benign juvenile melanomas from which it is possible to identify most of these lesions for what they are. Lesions in adult life are not infrequently erroneously diagnosed malignant melanomas, although they are actually benign juvenile melanomas that have persisted beyond puberty. Puberty is not necessarily the diagnostic demarcation. In other words, the histology of juvenile melanomas, as herein described, may transcend in application the fact that the patient is an adult.

Superficial melanocarcinomas, as herein defined, should be segregated from the more deeply invasive tumors for diagnostic as well as prognostic reasons. The superficial melanocarcinomas, as a group, have an appreciably better prognosis than the more deeply infiltrative tumors. Melanocarcinomas of mucous membranes—of the urogenital, anorectal, and head and neck regions—have an almost uniformly fatal prognosis. The absence of melanin in a tumor of mucous membranes is a completely unreliable basis for the exclusion of the diagnosis of melanocarcinoma. The junctional change is the diagnostic criterion of importance.

In a surprisingly high percentage of cases, five-year survival of a malignant melanoma is not equivalent to cure. A patient with a melanocarcinoma exhibits a diathesis for the activation of junctional nevi in various parts of the body but particularly in the vicinity of the primary tumor. This latter phenomenon is a contributory factor in local recurrences. Local recurrences as well as metastasis to regional lymph nodes do not preclude ultimate survival. The prognosis for cutaneous melanocarcinomas is better, to a remarkable degree, in women than in men. This fact is especially true for the tumors of the head and neck regions.

*Allen, A. C., and Spitz, S. To appear in Cancer 6: 1-45, 1953.*

# Carcinoma of the Skin

*Joseph J. Eller, M.D., and William D. Eller, M.D.*

Because of its accessibility, cancer of the skin offers opportunity for early diagnosis and adequate therapy. In no other location is it possible to obtain such satisfactory results. Despite this, there are many recurrences and a higher mortality than necessary, owing either to incorrect diagnosis or to inadequate therapy.

The destructive character of the growth may not be apparent for a long time, although the microscopic studies of the tissues may show typical cancerous changes from the onset. The temporary resting stages, absence of metastases, and the occasional spontaneous healing of the basal-cell type of cancer have led some to consider them benign. However, it must be assumed that all histologically proved skin cancers may endanger the life of the patient or be destructive to an adjacent organ, as the eyeball or the cartilaginous structures of the nose or ear.

The clinical and histopathological pictures seen in carcinoma of the skin may vary to a great extent. Many efforts have been made to correlate them and to distinguish a number of entities with characteristic clinical and microscopic findings. Lesions similar clinically, however, have been shown to have a different microscopic structure, and vice versa. A classification that has proved practical is one based on the type of cells composing the tumor regardless of their arrangement in the tissues. Thus, two main types of cutaneous carcinoma are readily distinguishable—the basal-cell carcinoma and the prickle-cell carcinoma. These fundamental types may be found mixed; either the cell elements comprising the growth may present an intermediate type between basal and prickle cells, or the basal and prickle cells may be seen together in the same tumor. Multiple

flat superficial epitheliomas, extramammary Paget's disease, and Bowen's disease because of their clinical and microscopic characteristics are placed in a special group of cutaneous carcinomas and may be considered "variants" that are treated similarly to basal-cell cancers but usually require more intensive therapy for their complete regression.

## Basal-Cell Carcinoma

The basal-cell carcinoma may arise from apparently normal or from previously altered skin. Clinically, its appearance varies with the age of the patient, duration, previous treatment, trauma, degree of reaction in the connective tissue, direction the neoplasm spreads, and such complications as ulceration or infection. These growths are found mostly after the fifth decade of life but they may occur at any age. They may be single or multiple. The sites of predilection are the face, particularly the temples, forehead, nose, and eyelids. When basal-cell carcinoma arises in apparently normal skin, it often begins as a small, shiny or scaly, gray or yellow or yellowish-red nodule that may be slightly elevated or within superficial layers of the skin or buried in the deeper parts. When the growth is deeper, the appearance of a flat or slightly retracted shiny spot, pink or salmon in color, which may be covered by tiny scales or crusts, may be seen. The nodular lesions tend to bleed on minimal injury, although they appear to be quite firm in consistency. After a time, the only visible sign may be a small superficial scar covering the affected site. The basal-cell cancer may retain these features, or mechanical erosion, bleeding, crusting, scaling, and scarring may recur intermittently. At

times, nodules similar to the original lesion may grow at its periphery or in the adjacent areas. Frequently, the primary nodule undergoes involution and the younger lesions surround the flat center, resembling a string of tiny pearls, or the secondary lesions may coalesce and frame the older central growth with a rolled, pearly border. Another type of growth results from proliferation of the primary lesion in all directions so that a globular nodule is formed. In summarizing, the following clinical types of basal-cell carcinoma are seen: flat, pagetoid, morphea-like, cicatrizing, ulcerating (rodent ulcers), nodular, papillary, and fungating. A purely "basal-cell carcinoma" (also called epithelioma) never metastasizes or does so only on the rarest occasions. We have never seen this happen and the rare cases reported are suspect.

### **Prickle-Cell Carcinoma**

The prickle-cell carcinoma is more dangerous because of its tendency to grow more rapidly, its capacity to infiltrate and to become fixed to the deeper tissues, and its ability to metastasize to the regional lymph nodes. It is most frequent in middle-aged or older persons but can occur at any age. It is found often in workers exposed to the actinic rays of the sun or to extreme heat or weather changes, such as farmers, sailors, and stokers. The most frequent sites are the cheeks, ears, nose, forehead, lips, dorsum of hands, mucous membranes of the tongue, the buccal mucosa, and the genitalia.

The course of the prickle-cell carcinoma varies greatly. In the early stages there may be no difference in its appearance from the basal-cell carcinoma. Some grow slowly and remain localized for years; others extend steadily within the skin and cause large defects. Still others may change suddenly from slow to rapid growths, infiltrate the underlying structures and metastasize to the regional lymph

nodes. Occasionally, some show extreme malignant qualities from the beginning.

### **Treatment**

During the past twenty years, our results have improved because of the added intensity and adequacy of treatment with the various methods used. Too much emphasis cannot be given to the importance of eradicating skin carcinomas by the first series of treatments. Inadequate therapy, whether with surgery or irradiation, results in residual disease requiring further treatment to effect a cure. Residual cancer cells may have a tendency to become increasingly resistant after successive attempts with insufficient therapy, and, moreover, such repeated procedures may accelerate the growth of the tumor.

In planning the therapy, the procedure should be determined by the following factors: histological type, rapidity of growth, location and size of the lesion, age and condition of the patient, whether the tumor was freely movable or fixed to the deeper tissues, and the presence or absence of palpable lymph nodes.

The therapeutic measures used in practically all of our cases were:

1. Surgery (scalpel, high-frequency knife or electrocoagulation).
2. Irradiation (roentgen rays or radium).
3. Combined surgery and irradiation.

Skin carcinomas have been treated by means of various caustic agents, such as acid nitrate of mercury, trichloroacetic acid, dichloroacetic acid, zinc chloride, etc. We too have tried some of these caustics on a few "basal cell" epitheliomas and found that the lesions can be destroyed by their use. However, we feel that their action was difficult to control and that recurrences were not uncommon.

In using radiation, we prefer roent-

gen rays wherever possible because of the ease of their application and the accuracy of dosage. Tumors in certain areas, however, such as the mucous membranes of the cheek, the nasolabial fold, the angle of skin between the ear lobes and the mastoid region, certain lesions on the tongue and lips, and some bulky skin tumors are more conveniently treated by means of radium tubes and plaques for surface applications and radium needles and radon implants (gold or platinum) for interstitial therapy. Using the Manchester System of computation, radium dosage can now be measured to give a fairly accurate equivalent in terms of roentgen units.

When radiation is used, a margin of surrounding apparently healthy tissue of from 3 to 10 mm. or more must always be included in the area exposed to treatment, the amount depending on the character, size, and location of the tumor. The same applies if electrocoagulation is used for destruction of the lesion or if the tumor is excised by scalpel or electrosurgery. The vast majority of carcinomas of the skin, less than 5 cm. in diameter and not more than 0.5 cm. thickness, can be completely eradicated by roentgen-ray therapy provided adequate doses are administered.

Our results have convinced us that the fractional dose method of roentgen-ray therapy is better than giving a single massive dose of 4000 or 5000 r. We prefer to give treatment in doses of 1000 r every day or every other day, for lesions less than 5 mm. in thickness, and for thicker lesions, 1500 r every other day. The massive dose technique

does not afford the safe latitude of skin tolerance as satisfactorily as fractionation. With fractionated roentgen-ray doses, the reaction in the skin is less, and the tissue tolerance is greater. There is less danger of overdosage; and repair, healing, and cosmetic results are decidedly better. The experience of the therapist who can observe the reaction to the treatments will help him determine the total amount of irradiation to be given in any particular case.

Most cutaneous malignant lesions are "basal cell" in type, especially those which appear on the face above the upper lip.

The prickle-cell type of carcinoma offers a much more serious problem. It requires more intensive irradiation for its complete eradication, and whether surgery or irradiation is to be used should be evaluated in the light of the cell structure seen on microscopic examination. Tumors having fully differentiated cells that are likely to be radioresistant are better treated by surgical measures, whereas those consisting of dedifferentiated, immature cells are usually more responsive to irradiation.

Because of the limitation of space, the details of irradiation dosage, technique of scalpel surgical removal, and that of removal or destruction of the various new growths by electrosurgical methods, have been omitted here. For these, as well as the management of carcinoma in special locations, such as the eyelids, lips, ear lobes, scalp, etc., and for therapy of the so-called "variants" of the basal-cell epitheliomas, the reader is referred to standard textbooks on tumors of the skin.

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Never refuse to see what you do not want to see, or what might go against your own cherished hypothesis, or against the view of authorities. These are just the clues to follow up, as is also, and emphatically so, the thing you have never seen or heard of before. The thing you cannot get a pigeon-hole for is the fingerpoint showing the way to discovery.

*Sir Patrick Manson (1844-1922)*

# Industrial Aspects of Cancer of the Skin

W. C. Hueper, M.D.

The demonstration of the occupational relation of cancer of the scrotal skin in chimney sweeps some 175 years ago provided the first evidence indicating that environmental agents are involved in the causation of human cancer. This original observation made during the era immediately preceding our present period of industrialization has since then been extended to many additional chemical and physical agents. Cancer etiology has been placed thereby on the basis of clearly demonstrable facts that can be profitably used in the diagnosis, therapy, and prevention of human cancer.

Excessive and usually prolonged exposure to the following agents sustained for occupational reasons and/or during work in a large and diverse number of industrial operations has resulted in the development of cancer of the skin or can be expected to exert such an effect.

## Agents

Chemical agents: arsenicals (inorganic and organic); combustion and distillation products of coal (coal tar, pitch, creosote oil, anthracene oil, soot); hydrogenation products of coal (heavy fractions of Bergius oils); distillation products of oil shale (shale lubricating oils, crude paraffin oils); processed petroleum products (fuel oils, lubricating oils, crude paraffin oils, petroleum tars, asphalt, pitch, coke, carbon black); combustion products of natural gas (furnace types of carbon black).

Physical agents: nonionizing radiation (ultraviolet radiation); ionizing radiation (roentgen-ray radiation and alpha, beta, and gamma radiation of radioactive substances of natural or artificial origin).

## Types of Contact

Contact with these agents may be continuous or intermittent and may occur not only for occupational but also for medicinal, dietary, or other reasons. Arsenic cancer of the skin, for instance, has been observed not only among miners of arsenic-containing ores (copper, zinc, silver), but also among smelter workers, insecticide and herbicide manufacturers, insecticide sprayers and dusters, orchardists, vineyard workers, farmers, and sheep-dip manufacturers. It has been found among consumers of wine or drinking water contaminated with arsenical-insecticide residues or arsenicals from smelter slag respectively and has been noted among patients who were given arsenic-containing medicines, particularly Fowler's solution. Likewise, cancer-producing exposure to coal tar, pitch, soot, creosote oil, petroleum tar, asphalt, coke, fuel oil, and crude paraffin oil has been sustained, not only by workers of the basic industries (coke-oven operations, gas plants, petroleum refineries), but also by those of secondary industries using, processing, or handling the basic products (tar refineries, briquet plants, cork-stone manufacturers, creosoting and wood-preserving plants, manufacturers of roofing tar, asphalt shingles, lamp black, paints, insulating materials, rubber, paper conduits, waterproof paper, carbon black, dry-battery cases, cordage, and crude paraffin). Additional groups of workers with effective contact to these carcinogenic combustion and distillation products of coal, petroleum, and natural gas are road-construction and repair men, roofers, textile workers, painters, machinists, mechanics, engineers, optical-

*From the National Cancer Institute, Bethesda, Maryland.*

lens grinders, carpenters, fishermen, chimney sweeps, stokers, and metal workers. The demonstration of 3,4-benzpyrene in the filtrates of the air of cities and of the exhaust of diesel and gasoline engines moreover suggests that there may exist a general environmental contact with carcinogenic hydrocarbons generated by the combustion of coal, fuel oil, diesel oil, and lubricants and fuel of gasoline engines.

Cancer of the exposed skin attributable to an excessive exposure to solar radiation and found particularly among fair-complexioned individuals working or residing in a dry and sunny climate or at high altitudes has been observed especially frequently in agricultural laborers, cowboys, ranchers, farmers, gardeners, lumbermen, nurserymen, orchardists, road workers, oil-field workers, rural mail carriers, railroad workers, engineers, fishermen, sailors, truck drivers, construction workers, prospectors, and herders. Similar exposures for non-occupational reasons may be sustained by outdoor sportsmen and inveterate sunbathers or may occur as the result of the excessive and very prolonged use of ultraviolet lamps for medicinal and cosmetic reasons.

The injudicious use of ionizing radiation (roentgen-ray radiation and radioactive chemicals) has resulted in a considerable number of cancers of the skin among radiologists, technicians, nurses, engineers, physicists, dentists, physicians, mechanics, and chemists. Similar untoward effects have been observed in patients who usually received repeated exposures to ionizing radiation for therapeutic or diagnostic purposes of malignant and nonmalignant conditions as well as among customers of beauty shops using roentgen-ray radiation for depilatory purposes.

Although claims recently have been advanced by several American investigators as to the apparent noncarcinogenicity of some of these agents (arsenicals, carbon black, lubricating oils) for population groups industrially exposed to them, such allegations are in-

variably the result of defective survey methods, highly incomplete medical records, and bad judgment. Environmental carcinogens are pathogenic wherever and whenever they are active in adequate intensity and duration. They, like the pathogenic micro-organisms, do not adhere to any specific and selective biological or sociological philosophy in such matters.

While for most cutaneous occupational carcinogens the contact with the skin is a direct one and the resulting cancers consequently develop in general within the exposed area (solar radiation: face, ears, neck, hands, forearms; roentgen-ray radiation and radioactive radiation: finger tips, hands, forearms, less often face and chest; coal tars, pitch, creosote oil, petroleum derivatives: face, ears, lip, neck, hands, forearm, scrotum, vulva), cancers following the deposition in the skin of ingested arsenicals often affect nonexposed parts, such as palms, axillary region, and trunk.

In most cases of occupational skin cancer there exists a long exposure and latent period before the cancers become manifest. It is especially noteworthy that the exposure to the carcinogenic agent may have ceased many years before the appearance of the resulting cancer. It is essential, therefore, to ascertain the complete occupational history of a patient with skin cancer whenever an attempt is made to determine a possible occupational or environmental causation of the tumor. The importance of this procedure is apparent from Table 1.

Since the symptoms of chronic skin damage by chemical carcinogens as a rule accompany or soon follow upon an exposure to these agents (arsenic dermatitis, tar and pitch dermatitis, oil dermatitis), they may have receded completely long before the cancer appears. The chronic radiation damage, on the other hand, may be very slow in development and may become occasionally manifest many years after the primary radiation injury occurred.

TABLE 1  
Latent Periods, in Years,  
of Occupational Skin Cancers

Agent	Average	Range
Arsenic		
Occupational .....	25	4-46
Medicinal .....	18	3-40
Tar .....	20-24	1-50
Creosote oil .....	25	15-40
Petroleum oil .....	50-54	4-75
Crude Paraffin oil.....	15-18	3-35
Radiation		
Solar .....	20-30	15-40
Roentgen rays .....	7	1-12

Thus, a chronic radiodermatitis may be seen without there having been at any time an erythematous effect if the individual doses were suitably small and properly spaced. Chronic radiodermatitis always accompanies the development of a cancer.

### Diagnosis

For the determination of an occupation-connected skin cancer, it is important not only to obtain definite evidence as to the nature and duration of the specific carcinogenic exposures sustained by the patient in his various employments but also to elicit information concerning the former presence of specific cutaneous reactions preceding the development of the cancer. Supporting evidence for the actual existence of a specific carcinogenic exposure should include, whenever possible, information on the occurrence of similar skin manifestations among fellow workers equally exposed. Whenever the development of a skin cancer may have been due to an exposure to air-borne cutaneous occupational carcinogens (arsenicals, tar and pitch fumes and dust, oil mist, radioactive dust), an excessive frequency of cancer of the lung may be demonstrable for the population to which the patient belongs. English occupational-cancer statistics have shown that not only the skin-cancer-incidence rate but

the total cancer-incidence rate for all sites is excessive for persons exposed to coal tar and pitch.

It is important from a clinical viewpoint to know that individuals who were exposed to industrial carcinogens affecting the skin frequently develop multiple cancers of synchronic or heterochronic occurrence. They, therefore, must be kept under constant medical observation for practically the rest of their lives, so as to eradicate newly formed cutaneous lesions while they are in a precancerous (hyperkeratotic, papillomatous) or early cancerous stage. This phenomenon is due to the fact that the cutaneous carcinogens produce a diffuse but latent cancerous transformation of the exposed skin from which local cancerous reactions arise at varying latent periods. There exists adequate and reliable evidence indicating that such developments sometimes may be hastened if the predisposed skin is subjected to some sort of nonspecific physical or chemical trauma, such as a burn or contusion. Such precocious and precipitous developments of cancers from a prepared soil following a trauma are the real basis of the alleged "acute traumatic cancers."

The available records on the frequency and number of industrial skin cancers in the United States are highly misleading as to reflecting the actual number and industrial distribution of occupational skin cancers occurring. While the chief inspector of factories and workshops of England and Wales lists every year more than 200 cases of epitheliomas (papillomas and carcinomas) caused by tar, pitch, oil, and arsenic among industrial workers, our own records show practically none despite the fact that identical hazards exist and unpublished cancerous responses have occurred among the American worker population. In a recent paper by Arhelger and Kremen on the arsenical origin of skin cancer, there were in a series of 110 skin cancers, nine traceable to previous medicinal exposures to

arsenicals. Since it may justly be assumed that non-medicinal contacts with similar arsenicals (occupational, dietary) exert an identical action on the skin and since such contacts are not infrequent for members of certain occupational groups as well as, to some extent, of the general population, it may be concluded that exposure to arsenic may play an important role in the production of skin cancer despite the existing lack of recorded evidence.

The available information on the causation of cancer of the skin from all sources indicates that the majority

of cancers of the skin are attributable to contact with specific environmental agents, including agents used by industry and manufactured by it for general consumption. The industrial aspects of cancers of the skin include, therefore, those relating to direct occupational exposures to industrial carcinogens of restricted groups of the worker population as well as indirect environmental exposures sustained by members of the general population to industrial carcinogens contained in consumer goods and in industrial wastes discharged into or deposited in the air, water, and soil.

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On October 23, in a joint ceremony at the Annual Dinner of the American Cancer Society, Dr. Charles Lund presented the Society's Award for Distinguished Service to Cancer Control to Dr. George N. Papanicolaou and Dr. Herbert F. Traut. Dr. Papanicolaou was honored for his pioneer studies in developing the technique of the cytological diagnosis of cancer. His studies of cells in normal and pathological conditions have been carried on since 1915. In 1928, his work had progressed so that he was able to diagnose cancer of the female genital tract from the study of exfoliated cells. Dr. Traut was honored with Dr. Papanicolaou for his successful and steadfast championship of the new diagnostic technique and for the important role that he, as a clinical gynecologist, played in securing widespread acceptance among doctors of the new method for finding unsuspected cancer. The fruitful collaboration between Dr. Papanicolaou and Dr. Traut culminated in the publication, in 1943, of the classic monograph "Diagnosis of Uterine Cancer by the Vaginal Smear." The Award is a silver medal. Both recipients of the award were presented with a medal and with an accompanying scroll.



# Precancers of the Skin

## Their Recognition and Management\*

Marion B. Sulzberger, M.D. and Victor H. Witten, M.D.

The terms "precancer" and "precancerosis" are admittedly impossible to define in precise scientific fashion. Obviously, in order to define "precancer," one must first be able to define "cancer."

The dread word CANCER means many different things to different people. But despite this, it is a generally accepted, useful term. It signifies not a particular disease, but a GROUP OF WIDELY DIVERGENT TYPES OF NEW FORMATIONS. In view of this great diversity in the characteristics of these tumors, one may well ask, "What then are the common features that justify their being lumped together under the one heading of cancer?" The answer, it appears to us, can be given about as follows: Cancer designates all those new growths that generally have in common such cardinal features of malignancy as the following:

1. Destructive growth with invasion of other tissues.
2. Progression with only extremely rare instances of complete spontaneous healing.
3. Formation of metastases.

Though by no means entirely satisfactory to the scientist or purist, this clinical definition will, we believe, come closer than any present histopathological or biological definition to including the tumors today generally termed "cancers" while excluding those now generally regarded as noncancerous.

Similarly, as Bruno Bloch pointed out more than twenty years ago, the most useful definition of a precancer is a clinical one. Precancerosis has meaning and usefulness only when it describes lesions that are grouped to-

gether on the basis of a vast clinical experience as to their common statistical prognostic features. A precancerosis is a type of lesion that, though not yet a true cancer, can on the basis of clinical statistics be predicted to give rise to cancer in a substantial proportion of instances within a roughly predictable period of time.

Since both the concept of cancer and that of precancer depend so largely upon clinical experience and clinical statistics, it is not to be wondered that the first suspicion and first step that can lead to effective diagnosis and treatment remains almost exclusively within the sphere of the clinician. Jonathan Hutchinson used the adjective "pre-cancerous" in 1882 to express the belief that cancer had a precancerous stage; and, although he may not have coined the word, his is the first use of it known to us. According to Dr. Bloch<sup>1</sup>, the noun "precancerosis" was first employed by Dubreuilh, in 1896, to designate a certain group of skin conditions. It has been largely the dermatologists who have described the entities, set up the criteria of diagnosis, developed and applied the indicated types of therapy, and indeed done much of the fundamental research, including the deliberate experimental production of precancers in laboratory animals. This is no doubt due to the fact that, though easily observed and studied when they appear on the skin or accessible mucous membranes, the precancers are mostly "asymptomatic" and thus generally escape detec-

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\*Illustrations, in color, are on page 200.



### PRECANCERS OF THE SKIN

Figure 1. Senile keratosis.

Figure 2. Senile keratosis with early malignant changes.

Figure 3. Chronic radiodermatitis.

Figure 4. Leukoplakia of buccal mucosa with beginning thickening of plaque.

Figure 5. Single, large lesion of Bowen's disease.

Figure 6. Early Paget's disease of nipple—THIS IS CANCER.



#### CANCER OF THE SKIN

Figure 7. Basal-cell carcinoma of lower eyelid.

Figure 8. Basal-cell carcinoma of lower eyelid.

Figure 9. Mixed-cell carcinoma of side of hand.

Figure 10. Basal-cell carcinoma of side of nose.

Figure 11. Squamous-cell carcinoma of tip of nose.

Figure 12. Basal-cell epithelioma.

tion by patient or physician when they originate elsewhere.

Nevertheless the circumstance that skin specialists have long been in the position to recognize certain lesions as being precancerous has undoubtedly prevented the occurrence of many millions of skin cancers. For many decades dermatologists have been able to include in their studies not only the clinical precancers of their patients but the deliberately produced experimental precanceroses elicited by various chemical and physical agents (arsenic, tars, roentgen rays, light, burns, etc.).

The wealth of clinical experience in regard to the statistical probabilities with which certain lesions—in themselves benign—will eventuate in cancers is naturally called upon daily in the practitioner's office. For no human being exists whose skin does not, at some time or other, present moles or other types of nevi and birthmarks, or freckles, skin tags, fibromas, keratotic and scaly patches, warty growths, fissures, superficial or deeper erosions, scars, small infiltrations, nodules, and innumerable other kinds of defects or excesses. Naturally the decision as to whether such lesions are precancerous—are, "to be or not to be cancers"—today represents one of the physician's most constant and weighty responsibilities. Particularly in dermatological practice, few days go by without the necessity of making such decisions—

sometimes with implications of scarring and disfigurement and even regarding life or death.

In pronouncing these far-reaching judgments, the physician should clearly recognize that he must rely principally on the clinical dermatological experience of the past—it is simply a fact that certain lesions in certain sites and under certain circumstances have been proved to possess substantial propensities to become cancerous—whereas other lesions (sometimes not a priori very different from the precancers in their microscopic or clinical characteristics) have been shown to possess far lesser tendencies to develop cancerous changes.

In Table 1 we attempt to separate three groups of common dermatological lesions on the basis of the probability of their becoming true cancers. It is hoped that the following all too brief sketches of some of the more common and important precanceroses in Group I may help the practitioner either to recognize or at least to suspect that a presenting skin lesion may be a precancer.

### Keratoses

*Senile keratoses* usually occur in the aged or predisposed (e.g., blue-eyed, blond, freckled, thin-skinned) persons who have been exposed to the sun and elements for many years. The com-

TABLE 1

### Lesions That May or May not Become Cancer

GROUP 1	GROUP 2	GROUP 3
Lesions most often becoming true cancers (precanceroses in the strict sense)	Lesions infrequently becoming true cancers	Lesions that generally remain benign
Bowen's disease Senile keratoses Cutaneous horns Leukokeratosis (thickened leukoplakia) Arsenical, tar, and oil keratoses Roentgen-ray sequelae of ulcerative and warty type Erythroplasia Xeroderma pigmentosum	Ordinary leukoplakia Chronic ulcerations or scars from burns, sinuses, or fistulas Kraurosis vulvae Sebaceous cysts Junctional nevi Seborrheic keratoses	Soft moles Hairy moles Freckles Ordinary café-au-lait spots Skin tags Warts, plane or vulgar Hemangiomas Noduli cutanei Corns Calluses

monly affected areas are the exposed parts—face, scalp, ears, and hands (Figs. 1, 2). The lesions are generally from 1 to 10 mm. in diameter, usually very slightly elevated, sharply circumscribed and scaly, and vary in color from reddish to light or dark brown, or even grayish-black. The scales, unlike those of seborrheic keratoses, are usually dry and adherent and when scraped off bleeding generally ensues.

*Arsenical keratoses* are another variety of precancerous keratoses. These usually result from prolonged exposure to arsenic in the form of arsenical medication or to arsenic in industry (plant sprays, insecticides, etc.) or foods, beverages, etc. Here the sites of predilection are the hands and feet, particularly the palms. The lesions begin as slow-growing, small, almost punctate or cornlike, warts that are hard and usually numerous.

### Radiodermatitis

When the changes that are produced in the skin by ionizing radiation, such as radium or roentgen rays, become clinically visible, they are known as radiodermatitis. Knowledge of the dates of exposure and the quality and quantity of radiation given is important in order to evaluate the significance of the **EARLY SKIN CHANGES**. These changes consist of erythema, edema, and sometimes denudation and ulceration. Should the ulceration persist, such an area should be excised and plastic repair done if necessary.

*Chronic radiodermatitis*, which may appear from a few to twenty or more years after the last radiation exposure, is first characterized by atrophy or scarring, mottled pigmentation and depigmentation, telangiectasia, scaling, and wrinkling (Fig. 3). The sequelae that appear later in the course of chronic radiodermatitis are the most important in regard to precancer and cancer and are those that require frequent observation and appropriate treatment. These sequelae are as follows:

Keratoses pinhead-sized or somewhat larger, firm, dry, and elevated lesions, which grow to become brownish, roughened, and even slightly verrucous lesions.

Ulcers, which may vary in size from a few millimeters to large dimensions. These are often extremely tender or painful and so torpid that spontaneous healing may never take place.

*Management.* Patients with chronic radiodermatitis should be observed every month to every six months and should always be instructed as to danger signs and to return at the "first sign of trouble."

Where exposure to the sun, on occasion, cannot possibly be avoided, sun "screening" preparations that incorporate both physical and chemical filtering agents should be used, providing, of course, they are well tolerated. Carefully selected creams and ointments should be applied to soften and relieve the dryness and "tightness" of the skin that usually accompany chronic radiodermatitis.

In addition, such patients should avoid unnecessary exposure to the sun and the rays of the ultraviolet lamp; and, of course, unless absolutely imperative, the affected areas should have no further exposure to ionizing radiation.

Biopsies should be taken whenever the slightest suspicion of cancer arises—even though this means repeated biopsy. If cancer supervenes, the lesion should be destroyed or excised and skin grafted if indicated.

### Leukoplakia

The mucous membranes of the cheeks and the anterior half of the dorsal aspect of the tongue are the areas most commonly affected. Vulvar leukoplakia is not uncommon after the menopause.

Early mild leukoplakia rarely becomes malignant but should be watched and treated if and as necessary. It is characterized by whitish or bluish-white spots, sharply outlined or fading into

the surrounding normal tissue. On the tongue, the papillae are obliterated. The lesions must be differentiated from mucous-membrane lesions of lichen planus and other dermatoses. These changes may remain quiescent or even regress somewhat. They are generally not to be considered precancers unless they tend to increase in thickness and extent (Fig. 4).

When the lesions become thickened, "heaped up," and verrucous and there is fissuring or ulceration, these must be considered as danger signals, since this type (LEUKOKERATOSIS) is more prone to undergo cancerous changes. Oral leukoplakia is more common in men than in women, the approximate ratio being 10:1.

### **Bowen's Disease**

This consists of a single lesion or an aggregate of small lesions of quite varying clinical appearance. As a rule they are sharply demarcated, somewhat elevated, slightly scaly, and of a pale-brown to brownish-red color (Fig. 5). After many years the lesions usually become verrucous, nodular, and/or ulcerative. The mucous membranes, particularly of the vulva, may be affected.

Bowen's disease must be differentiated from Paget's disease, superficial basal-cell epithelioma, erythroplasia, psoriasis, lupus erythematosus, lichen-planus-like drug eruptions, and other dermatological lesions.

### **Other Precanceroses**

For all further details concerning less common precanceroses, such as Queyrat's erythroplasia, xeroderma pigmentosum, Dubreuilh's melanotic freckles, etc., the reader must be referred to the available textbooks of dermatology.

### **Paget's Disease of the Nipple**

Paget's disease of the nipple is ACTUALLY CANCER and is always found associated with intraductal neoplasms;

some cases have axillary metastases when first seen. The treatment is RADICAL MASTECTOMY.

Early, it resembles eczematous dermatitis with redness, oozing, and crusting (Fig. 6). The eruption spreads slowly, despite antieczematous treatment, until the skin becomes red, moist, and ulcerated in spots. There is a gradual retraction of the nipple and, on palpation, superficial infiltration is usually felt.

While extramammary Paget's disease does occur, it is rare. Nevertheless, this occurrence indicates that the disease does not (as some have stated) necessarily always originate in the mammary glands. It is likely that, as Bruno Bloch has stated, Paget's disease has multilocular origins, including the lacteal glands and ducts and the related skin glands (e.g., apocrine glands, sebaceous glands, Montgomery's glands? sweat glands?).

### **Prevention**

Early recognition and correct therapy of precanceroses is of course a potent weapon in the prevention of cancer.

Moreover, the knowledge and exclusion of preventable causes or aggravating factors play a most important role in prophylaxis of both cancers and precancers.

Certain factors cannot be prevented by any means now available to the physician. These include the indubitable constitutional proclivity to develop certain types of precanceroses and skin cancers. This inborn tendency is evident in the fact that blue-eyed persons get skin cancers in much greater numbers than do brown-eyed swarthy individuals (according to Stephan Epstein, Fletcher Hall, and others, about six times as frequently). This is probably due to their greater susceptibility to the effects of light.

The dominant role of exposure to light and to the elements in the production of certain precanceroses and skin cancers is further evident in the

observations that persons in outdoor occupations (e.g., seafaring men, farmers, cowpunchers) and rural populations get such lesions much more frequently than persons in ordinary indoor occupations and city dwellers (about seven times as often). Moreover, the exposed parts of the skin (face, hands) develop precancers and cancers approximately 100 times more often than the areas generally protected by clothing. It has also been shown that the incidence of skin cancers throughout the world roughly parallels the annual number of hours of sunlight in a given place. For example, skin cancers occur about four times as frequently in the Dallas-Fort Worth, Texas, area as they do in Pittsburgh, Pa.

In addition to warning and protecting predisposed persons against chronic overexposure to the sun and elements, every effort must be made to prevent occupational, medicinal, and other overexposure of all persons to the long array of known common carcinogenic agents of modern life (oils, tar derivatives, ionizing rays, arsenic, etc.).

## Treatment

If treated early enough, precancers can usually be destroyed by any of several methods. Selection of the best method depends on many factors, e.g., nature of the particular lesion, its size and location, accompanying changes such as inflammation, infiltration and ulceration; previous treatment to area (e.g., roentgen rays, radium, or surgery), excessive exposure of site to sun, etc.

Table 2<sup>5</sup> summarizes the indications for radical and conservative treatment of various precancers.

If radical measures are required, the choice generally lies between surgical and radiological procedures that fall within the province of the respective specialties.

Local conservative treatment or superficial destruction can be accomplished by several means, the selection of which depends not only on the type, size, and site of the lesion but also to great degree on the particular experience of the physician.<sup>5</sup>

TABLE 2

### Classification of Skin Precancers According to Indications for Radical or Conservative Treatment<sup>a</sup>

Usually requiring only local conservative treatment or superficial destruction*	Usually requiring immediate surgical and/or radiologic intervention (whichever is indicated)
<ol style="list-style-type: none"> <li>1. Smaller areas of Bowen's disease</li> <li>2. Smaller areas of erythroplasia</li> <li>3. Small, flat, or only slightly elevated, noninfiltrated leukoplakia</li> <li>4. Kraurosis and leukoplakia of vulva, penis, etc., with only superficial lesions or erosions</li> <li>5. Roentgen-ray or radium sequelae, without infiltration or persistent ulceration</li> <li>6. Small senile keratoses without ulceration, infiltration or rapid growth</li> <li>7. Small lesions of these types without ulceration, infiltration or rapid growth</li> </ol>	<ol style="list-style-type: none"> <li>1. Larger and growing, infiltrated or ulcerated areas of Bowen's disease</li> <li>2. Larger and growing areas of erythroplasia</li> <li>3. Leukokeratosis (leukoplakia) of the ulcerating or papillomatous, infiltrated type</li> <li>4. Kraurosis and leukoplakia of vulva, penis, etc., with infiltration, ulceration, etc.</li> <li>5. Roentgen-ray and radium ulcers, with infiltrated advancing edges</li> <li>6. Senile keratoses, with beginning infiltration and ulceration, rapid growth, inflammatory reaction</li> <li>7. Arsenical, tar, oil, etc., keratoses, ulcers, nodules, infiltrated tumors</li> </ol>
Usually requiring only prophylactic measures and regular observation*	
<ol style="list-style-type: none"> <li>1. Moles and pigmented nevi (unless growing, infiltrated, or infected) may be destroyed by various methods or removed in toto if situated in areas subject to irritation.</li> <li>2. Small nonelevated leukoplakia (take care of teeth, correct vitamin deficiencies, search for allergy to oral products, examine for syphilis, forbid smoking, etc.)</li> <li>3. Scars from burns, etc. (except when showing persistent ulcers, infiltration, etc.)</li> <li>4. Roentgen-ray and radium, arsenic, oil and tar, etc. sequelae, of flat, nonulcerated, noninfiltrated, nonkeratotic type (telangiectasia, pigmentation, depigmentation, etc.)</li> </ol>	

\*When regional lymph nodes are palpable or when any other circumstance makes one suspect early malignant change, the expectant measures must be replaced by more radical treatment, and a biopsy must be made to establish the exact nature of the lesion.

One method is to freeze more superficial lesions with a pencil cut from solid carbon dioxide. Destruction with acid is also useful (e.g., trichloroacetic acid). The monopolar electrodesiccating current used together with thorough local curettage is an excellent method of treating most of the precanceroses, both deeper and more superficial. In selected cases, thorium X, a naturally occurring radioactive material that has been used in dermatology for almost forty years, has proved to be of value.

While it is true that the histological picture does not tell with certainty whether a lesion will become a cancer,<sup>2</sup> there are certain changes that, when taken in conjunction with the history and clinical findings do in their combination strongly suggest that a lesion is either a precancer or already a cancer

(e.g., irregular hypertrophy of the epidermis; abnormalities in mitotic figures; polymorphism of cells and particularly of nuclei; dyskeratotic manifestations; reactive inflammation in the cutis, etc.). Therefore, should there be a question regarding the clinical diagnosis of a particular lesion, and if the opinion of a specialist is not readily available, the general physician would do well to perform a biopsy and send an abstract of the history and a brief clinical description together with the tissue to a competent dermatohistopathologist or, if none such is available, to a general pathologist for preparation and microscopic diagnosis. Biopsies, when properly performed, generally cause little scarring. Furthermore, the consensus is that a correctly done biopsy will not hasten growth of a lesion or increase the danger of metastases.

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THE OLD MAN was thin and gaunt with deep wrinkles in the back of the neck. The brown blotches of the benevolent skin cancer the sun brings from its reflection on the tropic sea were on his cheeks. The blotches ran well down the sides of his face and his hands had the deep-creased scars from handling fish on the cords. But none of these were fresh. They were as old as erosions in a fishless desert.

From THE OLD MAN AND THE SEA by Ernest Hemingway; used by permission of the publishers, Charles Scribner's Sons.

# CANCER CLINICS

## Skin Cancer

**Case 1.** T. C., a 62-year-old banker, first seen in the Winship Clinic on May 23, 1952, came in complaining of a nodule on the left lower eyelid of one year's duration. A physician had been consulted for the first time one year ago; he incised the nodule but no fluid was obtained. Physical examination showed a healthy-appearing man. The skin of the face and hands was normal for his age. There were no other similar lesions. Local examination revealed a

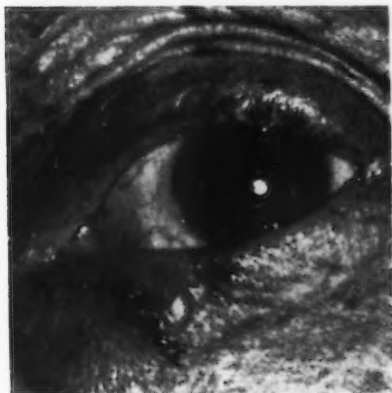


Figure 1. Case 1. Basal-cell type of epidermoid carcinoma.

nodule located in the skin just below the lid margins near the inner canthus of the left eye (Fig. 1). There was a well-circumscribed, superficial, nonulcerated, clear lesion, measuring 8 mm. in greatest dimension, that extended almost to the lid margin.

The entire lesion was excised. On pathological examination it was found to be a basal-cell carcinoma.

**REMARKS.** This is the typical manifestation of the basal-cell type of epidermoid carcinoma commonly found in this location, easily curable by surgery or irradiation when treated early, but locally destructive and maiming in the advanced stage. Distant metastases almost never occur.

The result was excellent.

**Case 2.** Mrs. M. P., a 53-year-old farm woman, first seen in the Winship Clinic on August 10, 1939, came in complaining of a "pimple" of the skin of the left cheek that was of several years' duration. There had been a recent rapid increase in size. No previous treatment had been given.

Physical examination showed a healthy woman with no positive findings except paralysis agitans. On local

*From the Robert Winship Memorial Clinic, Emory University Hospital, Emory University, Georgia.*

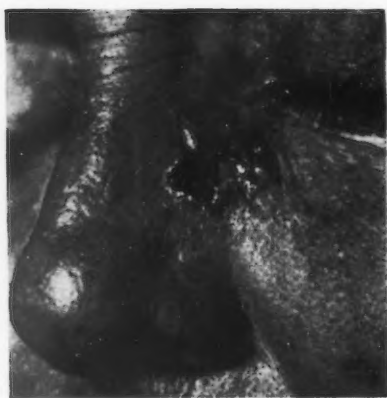


Figure 2. Case 2. Basal-cell epithelioma before treatment.

examination a poorly circumscribed, ulcerative lesion, with a pearly pink border, 2 cm. in greatest dimension, was found in the skin of the left infra-orbital region, extending up into the inner canthus of the eye (Fig. 2). The center was granular and bled easily when the crust was removed. It was movable and did not seem to involve the subcutaneous tissues. The lower punctum was not thought to be involved. A biopsy was taken with biting forceps from central area. On patho-



Figure 3. Case 2. Basal-cell epithelioma after treatment.

logical examination a basal-cell epithelioma was found.

Low - voltage roentgen - ray therapy was given using 0.6-cm. lead shield to protect the eye and surrounding tissues. A total of 1000 r  $\times$  3 was given at weekly intervals.

REMARKS. This was typical basal-cell epithelioma that had advanced to the stage of ulceration. It infiltrated out intraepithelially making it difficult to clearly demarcate the extent of the process. Since the underlying periosteum was not involved, the prognosis was expected to be good. The treatment of choice was irradiation, although other methods might be used with an expected good result. The intraepithelial extension and the nearness to the nasolacrimal system and lower eyelid favored the use of irradiation.

The result was a cure with minimal local change (Fig. 3).

**Case 3.** W. L. W., 63-year-old cotton-mill worker, was first seen in the Winship Clinic on March 21, 1942, complaining of a small lesion on the right temple of twenty years' duration. The patient stated that the nonulcerated nodule in the right temporal region began to increase in size rapidly eight months previously. It became infected and drained, formed a thick scab, and required regular dressings. He never consulted a doctor until his admission here. Physical examination revealed a fairly well-developed and nourished man. The general examination was noncontributory. Local examination showed a fairly well-circumscribed, ulcerative tumor, measuring 5 cm. in diameter, located within the hair, in the right temporal region. It was raised 1 cm. and covered by a crust that, when removed, showed irregular granular pink tissue. The border was firm, well circumscribed, and slightly rolled, and there is no evidence of intraepithelial extension. There was a suggestion of pigmentation at the border. It was moderately attached to the subcutaneous tissue and questionably attached to the temporal fascia. The

preauricular lymph node was not involved.

A biopsy of the granular area was taken with biting forceps. On pathological examination a basal-cell type of epidermoid carcinoma was found. Treatment was by excision and skin graft.

**REMARKS.** Clinically this appeared to be a basal-cell type of epithelioma, but the pigmentation suggested the possibility of a melanoma. The location suggested squamous-cell type, but the clinical appearance and absence of metastases favored the basal-cell type that was proved by biopsy. Treatment by surgery, excision, and skin graft was decided upon on the basis of the extent of the process and the amount of infiltration of subcutaneous tissues. Roentgen-ray therapy given over the skull in sufficient quantity to destroy the tumor frequently results in osteoradionecrosis of the outer table necessitating removal and long morbidity before skin-graft repair.

The patient has been well for ten years.

**Case 4.** F. C., a 39-year-old citrus worker, first seen in the Winship Clinic on January 29, 1946, complained of a tumor of the skin of the forehead of ten years' duration. The patient stated that ten years prior to admission he developed what he thought was a "seed wart" at the hairline on his left forehead. Six years ago he was in an accident and the entire wart was knocked off. It bled profusely and became secondarily infected. One year ago he received twelve roentgen-ray-therapy treatments. In the interim seven more roentgen-ray treatments were given, but the tumor never completely disappeared. One month ago he noticed a swelling of the preauricular lymph-node area and was referred by his radiologist to the Winship Clinic on account of this finding.

The physical examination was non-contributory. Local examination showed an ulcerative tumor, measuring 4 cm. in diameter, located on the skin

of the left forehead, at the hairline. Its border was raised almost 1 cm. in height and was rolled and hard and appeared active. It was slightly movable, but undoubtedly involved the full thickness of the scalp and was partially attached. The preauricular node was palpable and questionably involved. The cervical nodes were thought to be clear. Biopsies were taken at the active border. Pathological examination showed squamous-cell carcinoma, Grade II. Treatment: excision and skin graft.

**COURSE.** The patient lived at some great distance and did not return as planned until two months after the skin graft. At this time there was definite involvement of the preauricular lymph nodes, as well as multiple nodes in the left neck. On account of the extent of the disease it was felt that operative intervention was impossible, and therefore the patient was treated palliatively with roentgen-rays.

**REMARKS.** This lesion was a fairly typical high-grade squamous-cell carcinoma clinically and contrasts with that demonstrated in case 3. It was obviously a high-grade active process. Prophylactic dissection of the preauricular and left cervical lymph-bearing areas might have resulted in a cure, but the loss of time between the skin graft and first return visit afterward should not have occurred. In retrospect—clinical appreciation of the high activity of the primary tumor should have required earlier follow-up.

The result was death one year after the initial skin graft.

**Case 5.** R. F., a 53-year-old farmer, first seen on April 11, 1949, came in complaining of a growth on the dorsum of the left hand of two months' duration. The patient thought he got a briar in his hand and he tried to remove it, but without success. Shortly thereafter he noticed that the mass was increasing in size and it has rapidly developed in the last few weeks. The physical examination was noncontributory. Local examination showed the skin of the dorsum of the hand as soft



Figure 4. Case 5. Squamous-cell carcinoma, Grade I.

and healthy appearing; there were no other similar lesions. A pink, raised, small nodule involving only the skin and movable with it was located over the second metacarpal (Fig. 4). It measured 1.5 cm. in its greatest dimension. It was not ulcerated but was covered by a hard crust of dead skin that could not be separated from it. Examination of the suprachondral and axillary lymph nodes showed no enlargement or other suggestions of metastases. Treatment was by excision. Pathological examination showed squamous-cell carcinoma, Grade I.

**REMARKS.** Metastases are not common from this lesion but do occur to the epitrochlear and axillary nodes, which necessitates removal of the shirt and examination of these areas and subsequent follow-up visits. Treatment by surgery is preferable on the dorsum of the hand in all lesions more than 1 cm. in diameter, on account of the position and injury to tendons and periosteum over the metacarpals. A split-thickness skin-graft is frequently desirable.

The result was a cured patient.

**Case 6.** A. V. McC., a 56-year-old carpenter, first seen in the Winship Clinic on January 18, 1944, had multiple ulcerations on the hands and fingers. He stated that he had had an eczema

on both hands for many years and ten years previously he had been treated with roentgen-rays for the first time. He had immediate relief but had recurrences of the eczema after several months and has been treated intermittently with roentgen-ray therapy regularly until about one year ago. During this time he was warned by the radiologist that he was approaching his tolerance, but he admitted that he received so much benefit that he actually begged for further treatment. During the preceding year he had developed numerous keratotic spots on both hands that required constant dressings. The palms of his hands became dry and even the skin of the dorsum of the hands was fixed. He has applied many ointments without relief. General examination was normal throughout. Local examination showed the skin of both hands tight over the fingers and metacarpals. The nails were thickened and broken with numerous superficial ulcerations around them. There were numerous ulcerations on the fingers, discolored by the application of gentian violet. At the base of the right middle finger there was a definite ulceration that had never healed, the borders of which were hard and fixed. Biopsies of this area showed epidermoid carcinoma. Examination of the epitrochlear and axillary lymph nodes showed some enlargement, but the nodes were ovoid and soft and uniform to palpation. They were not thought to contain metastatic cancer; they probably had hypertrophied from the chronic drainage of the infected areas. Amputation of the right middle finger was done through the metacarpal. The ulceration at the base of left middle finger was excised and skin grafted. The pathological examination showed epidermoid carcinoma, low grade.

Patient developed a painful ulceration on the dorsum of the right hand requiring amputation. The axillary lymph nodes showed no change. The pathological examination revealed multiple epidermoid carcinomas.

The patient is living with multiple keratoses of left hand, which may eventually require amputation also.

Treatment of eczema of the hands with roentgen-ray therapy in the past has had disastrous results in many instances. The relief obtained at first encourages the patient to insist on treatments beyond the judgment of the physician in many cases.

**Case 7.** W. V. V., a 46-year-old marine engineer, first seen in the Winship Clinic on January 3, 1952, complained of an ulceration of the left scapular region of several months' duration. He had received a severe burn in 1915. He was advised to have a skin graft and was warned that he might develop cancer, but he disregarded this advice and thought he had triumphed when the ulceration finally healed three years before being seen in the Winship Clinic. Three months prior to his first visit he developed a recurrence of the ulceration of the left scapular area and two months prior noticed a painful mass in the left axilla. This was drained and a large amount of pus evacuated. The pain became so severe that he had resorted to the use of narcotics and alcohol. On physical examination the patient seemed to be fairly well developed and nourished but was obviously under the influence of a narcotic. The history was given by his wife. The general examination was otherwise noncontributory. Local examination showed a diffuse scarring over the entire back with involvement of the posterior axillary folds on both sides, typical of the late effects of a burn. There was a large ulcerative area in the center of the posterior axillary fold that measured 8 cm. in its greatest dimension. The pale granular tissue in the center of the ulcer was typical of carcinoma, and there was much secondary infection and pus. The left axilla was swollen with masses, one of which was draining pus on pressure. The most painful larger one had not broken down. There was no evidence of extension of the process above the clavicle from the ax-

illa, which was thought to be completely involved by metastatic disease. The left arm was smaller than the right, probably because of lack of use. Biopsies of the ulceration in the burned scar were done and epidermoid carcinoma, Grade II, was found. Treatment was by excision of the burned scar, axillary dissection, and massive skin graft. The pathological examination of the lymph nodes showed epidermoid carcinoma, Grade IV, very anaplastic.

The patient did remarkably well and eventually healed without evidence of recurrence so far. The prognosis is guarded, with a chance of cure not good.

### Summary

The great majority of skin cancer occurs on the exposed surfaces of the head, neck, and hands. Only rarely is it found on the trunk and lower extremities. Skin cancer, more than any other type of cancer, should offer the highest rate of prevention, diagnosis, and cure, yet the mortality and morbidity caused by it are of considerable magnitude. An understanding of the life history of epidermoid carcinoma in its various locations is of fundamental importance. The locally infiltrating characteristics of the basal-cell type, the complications of intraepithelial extension, and involvement of cartilage, mucous membrane, and periosteum offer serious obstacles to eradication and frequently result in impaired function and disfigurement. The basal-cell type rarely metastasizes.

Squamous-cell carcinoma of the skin metastasizes to the lymph nodes, but an appreciation of its true potentialities must be understood in order to protect the patient from unnecessary treatment in the name of prophylaxis and at the same time anticipate the possible complications. Lymph-node metastases are relatively rare from skin cancer and certainly the least common of any anatomical location where epidermoid carcinoma occurs.

Many times it is possible to distinguish the basal-cell from the squamous-cell type on clinical examination with the definite advantage of arriving at a correct treatment immediately. However, some epidermoid carcinomas are indistinguishable and indeed one cannot be sure of epidermoid carcinoma in some skin lesions until biopsy examination. Histological diagnosis is desirable in all cases whether obtained by biopsy or examination of the specimen for either immediate management or subsequent follow-up.

Prevention comes from protection of susceptible skin from undue exposure to direct actinic or radium and roentgen-ray radiation, the application of skin grafts to second- and third-degree burns, and the eradication of active keratoses.

Cure depends most on the thoroughness of the first treatment after the diagnosis is made, whether roentgen-rays, radium, or surgery is used. Selec-

tion of the best of these methods may be equivocal in some cases, but general statements can be made concerning the advantage of both methods, whether used separately or in combination. Radiation is usually preferable on small and multiple lesions and where there is sufficient subcutaneous tissue. It should not be used on the extremities or where bone and cartilage or tendons may be injured, excepting possibly on small and superficial lesions in these locations. Surgery is usually preferable on the large, bulky tumors and in those areas where radiation is not desirable. In combination, surgery is used in instances after radiation has obtained its maximum effect and in other cases radiation is used for small recurrent areas after wide surgical extirpation. Surgery is usually preferable in the curative treatment of metastases from skin cancer, but radiation is invaluable as a palliative measure and indeed some of these attempts result in cure.

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THE BETATRON that was installed at Memorial Cancer Center in October, 1952, is the second in the country to be used for medical research and the first designed specifically for this purpose. It produces 20 to 26 million electron volts and is approximately ten to thirteen times more

powerful than the most powerful of the conventional roentgen-ray machines. It is hoped that these higher energy roentgen rays will permit the delivery of greater doses of radiation to deep-seated cancer tissues with minimal damage to the skin and normal tissues through which the beams must also pass. This should be possible, since the roentgen rays emitted by the Betatron build up to maximum intensity after they have entered the body, rather than at the level of the skin and superficial tissues. The Betatron can also emit beta rays, which, in contrast to roentgen rays, terminate abruptly rather than penetrating and scattering within the body. The depth to which the electron beam will penetrate can be controlled by varying the energy of the Betatron.

The Betatron will be used to try to treat localized internal cancers that cannot be destroyed by present surgical or conventional roentgen-ray methods. In addition, it provides a valuable tool for study of radiation effects on various parts of the body because the amount of radiation delivered to a given volume of living tissue can be very accurately controlled and determined.



## DOCTORS DILEMMAS

**Q** *A 22-year-old woman had a small nodule removed from the right breast. Histologically it was shown to be non-malignant. Two years later subcutaneous nodules appeared at the site of the incision. Biopsy showed perineural fibrosarcoma. Radical mastectomy was performed. No residual tumor was found in the breast or axillary lymph nodes. The patient is now pregnant. Since her sarcoma was of the slow-growing and locally invasive type, should pregnancy be terminated?*

**A** No. Pregnancy may be permitted to continue since there is no evidence that the hormones or any other factor in pregnancy will cause recurrence of fibrosarcoma.

**Q** *Have standards been formulated to outline the maximum permissible exposure to roentgen rays for humans?*

**A** Early protective measures against irradiation damage are purely empirical, delayed by lack of a method for accurately measuring ionizing radiations. It is known that small doses of irradiation may produce irreversible and cumulative changes that may appear, as with skin changes, as long as twenty-five years after exposure to irradiation ceases. The International Commission on Radiological Protection recommends as maximum permissible exposure to the whole body or gonads an amount not in excess of 0.3 r per week measured in free air (0.5 r on the body surface), or 1.5 r per week in the case of hands and forearms. The maximum permissible exposure figures quoted refer to externally originating roentgen


or gamma rays of quantum energy less than three million electron volts.

**Q** *How potentially malignant is the so-called benign bladder papilloma when treated with fulguration?*

**A** Of 100 unselected patients with "benign bladder papilloma," treated by fulguration, fifty-three are alive and well for from five to twenty-eight years after the first treatment. Thirty-four of the group died of conditions unrelated to papilloma, after having lived an average of twelve and a half years. Ten of the group developed cancer within two to ten years after the first treatment, and three had cancer of the bladder when first seen.

**Q** *Is it correct that the incidence of cancer of the female breast is less during menopause than during the years before or after?*

**A** Statistics from several centers both in this country and in Europe, show that there is a leveling off or even actual decrease in breast-cancer incidence between the ages of 50 and 54. The rate rises sharply from the ages of 25 to 29 to 45 to 49, and rises sharply again between 55 and 64, after which the increase is somewhat slower. The leveling off between the years 50 and 54 approximates the years of the menopause according to other studies, which indicate that 45 per cent of women have the menopause between the ages of 48 and 50 and that 88.6 per cent of women cease menstruating between the ages of 45 and 53.



# new developments in cancer

## **Cancer Prophylactic . . .**

Salter of Yale University School of Medicine has recommended "prophylactic" use of radioactive iodine in surgery for thyroid cancer. His results indicate that the iodine collects on the surgical wound and destroys cancer "crumbs" that might be deposited there.

## **Doesn't Prolong Life . . .**

ACTH and cortisone, which have wrought some dramatic but temporary remissions in acute leukemia, probably don't prolong the lives of the patients. This was the conclusion of Bassett and associates at the University of California at Los Angeles in a survey of their experience with the hormones. They also found that good effects of the drugs end shortly after withdrawal.

## **Prevention of Chemical Carcinogenesis . . .**

Moon, Simpson and Evans (University of California) found hypophysectomy to protect rats against methylcholanthrene carcinogenesis. Pellets of this carcinogenic chemical were implanted into the gastrocnemius muscle of 15 rats, 8 of which developed rapidly

growing sarcoma in from 195 to 299 days. Only one of 15 hypophysectomized rats similarly treated with methylcholanthrene developed sarcoma at the implantation site. Previous work in this laboratory had shown the importance of the pituitary in neoplastic disease since diverse neoplasms developed in the rat following the prolonged administration of growth hormone and since spontaneous tumors and those induced by growth hormone do not occur in the hypophysectomized rat. This new work — inhibition of methylcholanthrene carcinogenesis by hypophysectomy — adds another link to the chain of evidence concerning the relation of the endocrine system to neoplastic disease.

## **Radioiodine Cautions . . .**

A word of caution on the use of radioactive iodine in treatment of Graves's disease is issued by Corrigan and Hayden of Harper Hospital, Detroit. They report that while radioiodine with their techniques (involving longer and more difficult tracer studies than those generally practiced) is invaluable in diagnosis of thyroid cancer, improper use of the isotope as therapy for Graves's disease may cause cancers.

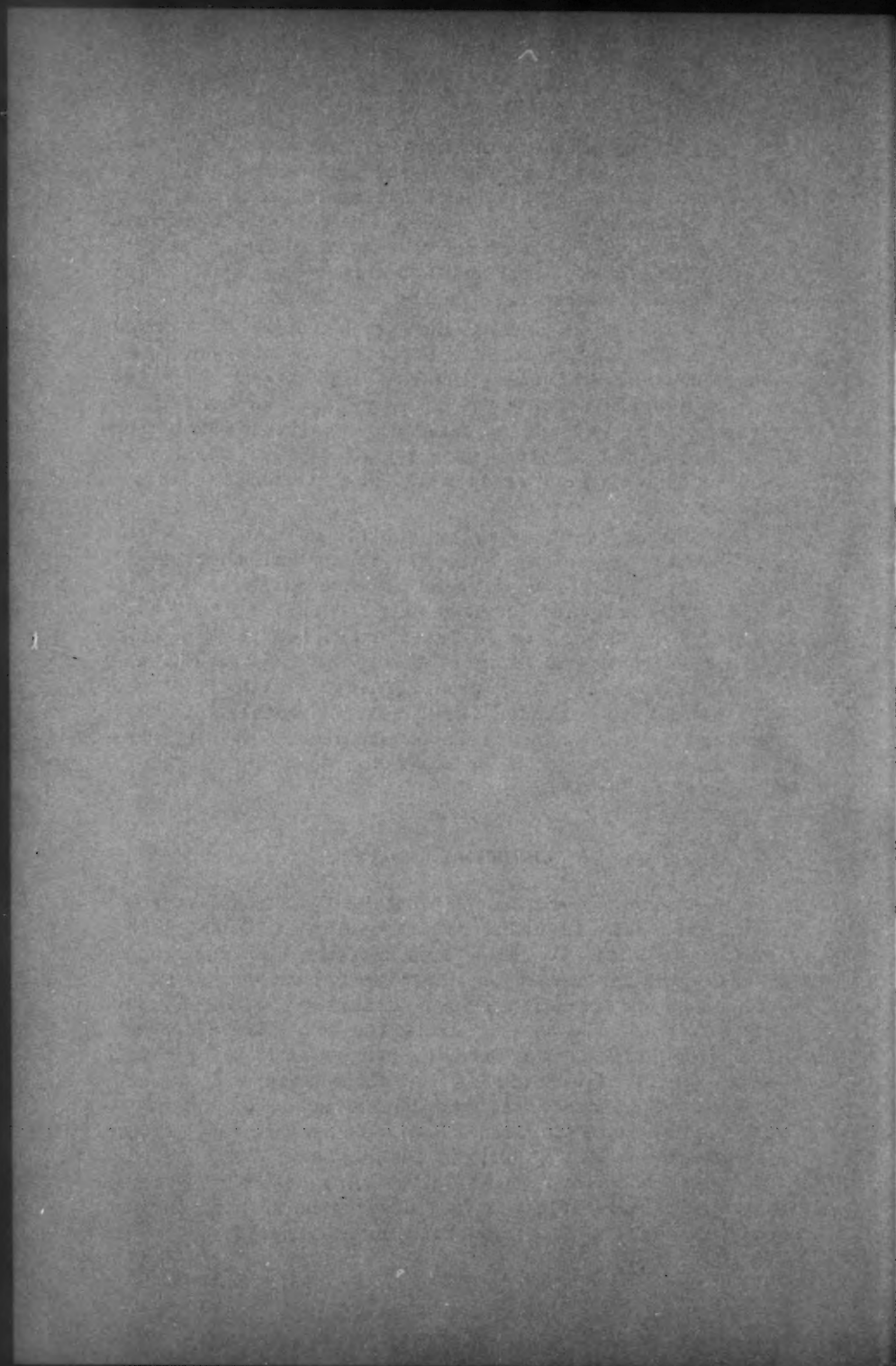
Sulfapyrazine concentrated strongly in transplanted Walker rat tumors in tests by Stevens and others at the University of Cincinnati College of Medicine. Concentrations were higher in tumors (especially in necrotic material) than in serum of other tissues in almost half the tumors. Rats were sacrificed about four days after injection. The procedures were generally lethal.

Female cockroaches last much longer than males under starvation conditions, Scharrer of Colorado found. Lethal cockroach abdominal tumors follow severing the sympathetic nerve supplying the salivary sac. Ordinary males survived twice as long as females. An inquiry into possible nutritional factors showed that females spent their foodless days quietly while males used themselves up in a restless quest for food.

The sanitary drinking habits of insects -- they spread a mild antibiotic over the wound when they bite -- has brought to light a compound of interest in cancer research. The compound is sanguinin, an antibiotic. Anigstein of the University of Texas extracted it from human and animal blood; and Cline of the Medical College of Alabama is testing its biological effects. Cline has found that the compound reduces synthesis of catalase. Liver catalase is drastically reduced in almost all kinds of human cancer. Sanguinin or a similar compound may supply the mechanism for this.

#### CHILDREN'S CANCERS

A pamphlet entitled, "Just What is the Children's Tumor Registry?" is being distributed to 165,000 physicians in the United States. Dargeon of the American Academy of Pediatrics has completed a statistical survey and coding of 583 cases and drawn up a chart indicating the histological distribution of the cases. Among the more common types of cancer in children and their percentages are: the leukemias (24 per cent), lymphatic -- including Hodgkins disease, lymphomas, lymphosarcoma, and reticulum-cell sarcoma -- (9.1); osteogenic sarcoma (8.6); neuroblastoma (10.5); retinoblastoma (8.1); Ewing's tumor (7.9); Wilms's tumor (4.6), and rhabdomyosarcoma (3.9). The Registry has published persuasive evidence that physicians should consider cancer in hard-to-diagnose children's ailments.



## International Classification of the Stages of Carcinoma of the Uterine Cervix

Because of the continuing interest in the International Classification, reprinted from CA, vol. 1, pages 84-85, 1951, a second printing has been made. Requests for copies will be filled upon receipt.

## COMING MEDICAL MEETINGS

Date	Association	City	Place
1953			
Jan. 7-19	Pan American Medical Association	Cruise—Nieuw Amsterdam	
Jan. 22-24	International Postgraduate Medical Association—S. W. Texas	San Antonio	Auditorium
Feb. 4-6	Philadelphia County Dental Society	Philadelphia	Bellevue-Stratford
Feb. 8-11	Chicago Dental Society	Chicago	Conrad Hilton
Feb. 9-12	Inter-American Session, American College of Surgeons	Sao Paulo, Brazil	Paulista Medical Association Bldg.
Feb. 10-13	Mid-South Postgraduate Assembly	Memphis	Peabody
Feb. 23-25	Atlanta Graduate Medical Assembly	Atlanta	Atlanta-Biltmore
Mar. 2-5	New Orleans Graduate Medical Assembly	New Orleans	Auditorium
Mar. 3-6	Chicago Medical Society Annual Clinical Conference	Chicago	Palmer House
Mar. 9-12	Southeastern Surgical Congress	Louisville	Brown
Mar. 11-13	Michigan Clinical Institute	Detroit	Sheraton-Cadillac
Mar. 16-19	Dallas Southern Clinical Society	Dallas	Adolphus and Drake Hotels
Mar. 23-26	American Academy of General Practice	St. Louis	Kiel Auditorium
April 6-10	Federation of American Societies for Experimental Biology	Chicago	Conrad Hilton
April 7-9	American Association of Railway Surgeons	Chicago	Drake
April 9-11	American Association for Cancer Research	Chicago	Drake
April 13-17	American College of Physicians	Atlantic City	Convention Hall
April 21-23	Ohio State Medical Association	Cincinnati	Netherland-Plaza
April 21-24	Industrial Medical Association	Los Angeles	Statler
April 26-29	Texas Medical Association	Houston	Shamrock
April 27-30	Connecticut State Medical Society	Hamden	Hamden High School
April 28-May 1	Philadelphia County Medical Society	Philadelphia	Bellevue-Stratford

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